Benzhexol Tablets

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

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Further follow-up action as required.	

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Change **to**: **Benzhexol Tablets**

Benzhexol Hydrochloride Tablets; Trihexyphenidyl Hydrochloride Tablets

Benzhexol Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of benzhexol hydrochloride, $C_{20}H_{31}NO,HCl$.

Usual strengths. 2 mg; 5 mg.

Identification

A. Disperse a quantity of the powdered tablets containing 20 mg of Benzhexol Hydrochloride with 20 ml of *water* and filter. The filtrate yields a yellow precipitate with *trinitrophenol solution* and a white precipitate with *5 M sodium hydroxide*.

B. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

Tests

Dissolution (2.5.2).
Apparatus No. 1 (Basket),
Medium. 900 ml of acetate buffer pH 4.5, prepared by dissolving 3.0 g of *sodium acetate* and 1.7 ml of *glacial acetic acid* in 1000 ml of *water*, adjusted to pH 4.5,
Speed and time. 100 rpm and 45 minutes.

Withdraw a suitable volume of the medium and filter.

Bromocresol green solution. Dissolve 125 mg of *bromocresol green* in a mixture of 10 ml of *water* and 2.5 ml of *0.1 M sodium hydroxide,* dilute to 250.0 ml with the dissolution medium, mix and extract twice with 100 ml of *chloroform* and discard the chloroform extract.

Test solution. Use the filtrate, dilute, if necessary, with the dissolution medium.

Reference solution. Dissolve a suitable quantity of *benzhexol hydrochloride IPRS* in the dissolution medium and dilute with the dissolution medium to obtain a solution of the similar concentration as that of the test solution.

Transfer an accurately measured volume of the test solution containing 50 µg of Benzhexol Hydrochloride, an equal volume, each of, the reference solution and the dissolution medium (as blank) to three separate 50-ml centrifuge tubes. Add 5.0 ml of bromocresol green solution and 10.0 ml of *chloroform* to each tube, insert the stoppers into the tubes and shake vigorously for 20 seconds. Centrifuge the mixtures to separate the layers. Aspirate and discard the upper aqueous layer. Filter each chloroform layer through a separate phase-separating filter paper. Measure the absorbance at the maximum at about 415 nm (2.4.7). Calculate the content of $C_{20}H_{31}NO,HCl$ in the medium from the absorbance obtained from the test solution and the reference solution.

Q. Not less than 75 per cent of the stated amount of $C_{20}H_{31}NO,HCl$.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 80 volumes of *methanol* and 20 volumes of *water.*

Test solution. Disperse a quantity of powdered tablets containing 25 mg of Benzhexol Hydrochloride in 2.5 ml of *0.1 M hydrochloric acid* with the aid of ultrasound, add 20 ml of mobile phase B, sonicate again and dilute to 25.0 ml with mobile phase B. Centrifuge and use the supernatant.

Reference solution (a). A 0.0001 per cent w/v solution of *benzhexol hydrochloride IPRS* in the solvent mixture.

Reference solution (b). A solution containing 0.01 per cent w/v of *benzhexol hydrochloride IPRS* and 0.001 per cent w/v of *benzhexol impurity A IPRS* in the solvent mixture.

Chromatographic system

- a stainless steel column 10 cm x 2.1 mm, packed with octadecylsilane bonded to porous silica (2.6 µm) (Such as Kinetex XB-C18),
- mobile phase: A. a buffer solution prepared by dissolving 1.4 g of *potassium dihydrogen phosphate* in 1000 ml of *water*, adjusted to pH 4.0 with *orthophosphoric acid*,
  B. dilute 0.5 ml of *orthophosphoric acid* to 1000 ml with *acetonitrile,*
- a gradient programme using the conditions given below,
- flow rate: 0.3 ml per minute,
- spectrophotometer set at 210 nm,
- injection volume: 3 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	95	5
20	60	40
22	60	40
22.1	95	5
24	95	5

Name	Relative retention time
Benzhexol impurity A*	0.4
Benzhexol	1.0

*Process impurity included for identification only and is not to be included in the calculation of total degradation products.

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to benzhexol impurity A and benzhexol is not less than 2.0 in the chromatogram obtained with reference solution (b), the relative standard deviation for replicate injections is not more than 2.0 per cent and the signal-to-noise ratio is not less than 50 in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any secondary peak is not more than 10 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent) and the sum of the areas of all the secondary peaks is not more than 20 times the area of the principal peak in the chromatogram obtained with reference solution (a) (2.0 per cent). Ignore any peak with an area less than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent).

Uniformity of content. Complies with the test stated under Tablets.

Determine by liquid chromatography (2.4.14) as described under Related substances with the following modifications.

Test solution. Disperse one intact tablet in *0.1 M hydrochloric acid* (10 per cent of the final volume), with the aid of ultrasound and dilute with mobile phase B to obtain a solution containing 0.02 per cent w/v of Benzhexol Hydrochloride, centrifuge and dilute 5.0 ml of the supernatant to 10.0 with the solvent mixture.

Reference solution. A 0.01 per cent w/v solution of *benzhexol hydrochloride IPRS* in the solvent mixture.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 3.0 and the relative standard deviation for replicate injections is not more than 1.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{20}H_{31}NO,HCl$ in the tablet.

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14), as described under Uniformity of content with the following modifications.

Test solution. Weigh and powder 20 or more tablets. Disperse a quantity of the powder containing 50 mg of Benzhexol Hydrochloride in 10 ml of *0.1M hydrochloric acid* with the aid of ultrasound and dilute to 100.0 ml with mobile phase B. Centrifuge and use the supernatant. Dilute 5.0 ml of the supernatant to 25.0 with the solvent mixture.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 3.0 and the relative standard deviation for replicate injections is not more than 1.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{20}H_{31}NO,HCl$ in the tablets.

Storage. Store protected from moisture, at a temperature not exceeding 30°.